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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/521,742	03/09/2000	Lars Hammarstrom	49122	2762

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/521,742	HAMMARSTROM ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Arguments

1. Claims 28-57 are pending.

Claim 50 has been amended.

Claims 1-27 have been cancelled.

Claims 28-57 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Oath/Declaration

3. The declaration under 37 CFR 1.132 filed September 29, 2003 is insufficient to overcome the rejection of claims 27-57 based upon the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the said claims as set forth in the last Office action because: the reasons set forth below in paragraph 5.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

4. The rejection of claim 50 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the claim amendment.

Maintained Rejections

Claim Rejections - 35 USC § 112

5. The rejection of claims 28-57 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating malignant cancer cell lines (such as those listed in Table 1 of the specification, see page 26) by contacting the said cells with an enamel matrix derivative, namely EMDOGAIN® thereby inducing apoptosis, does not reasonably provide enablement for a method for treating epithelially/ectodermally derived benign, semi-malignant or malignant, comprising administering to a mammal an active enamel substance is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants draw the Examiner's attention to the MPEP and the provisions of 35 USC § 112 setting forth that "[o]ffice personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials" and the requirements of 35 USC § 112 are distinct from those of the Food and Drug Administration, respectively. Applicants have submitted a declaration under 37 C.F.R. § 1.132 surmising several attributes of the product to be used in the claimed invention. All of these points of view, as well as the declaration have been carefully considered, but found unpersuasive.

On page 1 of the declaration Applicants submit that "[i]t is as of today not clearly proven, which of the ...mentioned proteins or cleavage products of them, comprised in

the enamel matrix actually constitute[s] the active fraction". And while Applicants are proper in their recitation of the 112 statute in that it does not require absolute predictability with respect to the practice of every possible embodiment of a claimed invention, the MPEP with particularity section 2164.08 sets forth that "[T]he record must be clear so that the public will have notice as to the patentee's scope of protection when the patent issues". Applicants' claims, as well as the specification are remiss in the identification of constituents comprised within the active enamel substance, which is germane to the *in vivo* implementation of the claimed invention. Applicants have not provided sufficient guidance that would allow one of ordinary skill in the art to know they have the active substance or what analysis should be executed in order to definitely assess the proper constituents that should comprise the active substance for use in the claimed invention.

The declaration attests to the "the active enamel substance for inducing apoptosis in a targeted neoplasm should optimally comprise a molecular weight of up to about 40,000, but no more than 60,000 Daltons, see page 2 of the declaration. However, the claims read on a method for treating targeted neoplasms with an active enamel substance with a molecular weight less than 60 kDa, for instance 5 and 25 kDa. Furthermore, the declaration states that examples 2 and 3 within the specification prove the apoptotic effect of a composition comprising the lower molecular weight of an enamel matrix. The Examiner has reviewed the examples set forth on pages 23-25, Figures 1-3, as well as the figure descriptions provided on page 20 and there is no reference as to what constituents comprised the enamel matrix and no indication what

the weight was of the said matrix. Dr. Lyngstadass' statement does not advance the enablement of the claimed invention and is not commensurate with the limitations of the dependent claims.

In conclusion the declaration states, "...the effect demonstrated *in vitro* is highly indicative of the effect that ...said enamel proteins will have in the clinical situation ...envisioned in the application." This extrapolation seems to be based upon situations not clearly and definitely outlined. The data set forth in Table 1 (page 26), as well as Figures 1-3 just show an increase in induced cell death in the presence of EMD in the cell cultures with no information governing how much EMD was applied or what the mixture of enamel substances comprised. The information gleaned from these observations suggests that given enough time EMD may induce apoptosis. Nevertheless, there continues to be insufficient guidance on the pharmacokinetics regarding any and all active enamel substances to be administered which is necessary for one of skill in the art to practice the invention in order to achieve predictable results.

Due to the unpredictability of therapeutics, the absence of any evidence concerning the effectiveness of the undefined composition comprising a plethora of enamel substances as a pharmacological agent, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the claimed invention with a reasonable expectation of success. The quantity of experimentation necessary to determine whether or not any active enamel substance is capable of preventing or treating any malignant or benign neoplasms is infinite.

5. The rejection of claims 28-57 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

Applicants argue that the terms are clearly defined in the present application and would be readily understood by the skilled artisan. In support of the traversal to the instant rejection Applicants point out wherein the specification relevant disclosure is found. The arguments and specific sections of the specification have been reviewed and considered, but found unpersuasive.

a. The recitation " therapeutically effective amount of an active enamel substance" in claims 28-41, 43, 47, 48 and 52-57 are vague and indefinite. As based on the scope of enablement rejection set forth above it not clear what amount is considered an effective amount and how it is considered therapeutic. The rejection is maintained for the said reasons and those set forth in previous Office actions. The metes and bounds continue not to be determined.

b. Claims 30, 30 and 46 are vague and indefinite in the recitations " enamel matrix derivatives", "derivatives thereof" and "mixtures thereof". Applicants have not set forth specific combinations of all the enamel substances, combinations, percentages of the different substances that comprise the derivatives and mixtures. Passages of the disclosure that suggest that 90% of the substance is X or Y is not sufficient in overcoming the rejection. The metes and bounds continue not to be determined.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4315.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
17 December 2003